# THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

TWELFTH EDITION

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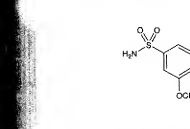
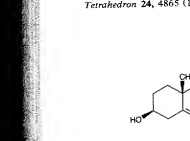
naud, J. Macler, *ibid.* 57, 353 (1981); S. Angeli, P. Fougère, *ibid.* **58,** 111 (1982).



THERAP CAT: Treatment of menopausal disorders.

**10082. Veralkamine.** *(3ß,16ß,17α,22α)-17-Methyl-18-nor-16,28-secosolanid-5,12-diene-3,16-diol; 17-methyl-20α-(12S,5S)-5-methyl-2-piperidyl)-18-nor-17α-pregno-5,12-diene-3ß,16ß-diol;* (22S,25S)-12,26-epimino-17ß-methyl-18-norcholesta-5,12-diene-3ß,16ß-diol; (17S,12S,25S)-22,26-epimino-18(13→17)-*abeo*-cholesta-5,12-diene-3ß,16ß-diol; veralcamine. $C_{27}H_{45}NO_2$: mol wt 413.64. C 78.40%, H 10.48%, N 3.39%, O 7.74%. Steroidal alkaloid isolated from *Veratrum album* ssp. *lobelianum* (Bernh.) Suessenguth, *Liliaceae:* Tomko *et al., Pharm. Zentralhalle* **99,** 373 (1960); *C.A.* **55,** 2013e. Structure studies: Tomko *et al., Coll. Czech. Chem. Commun.* **27,** 1404 (1962). Complete structure: Tomko *et al., Tetrahedron Letters* **1967,** 3907; *eidem, Tetrahedron* **24,** 4865 (1968); Hoehne *et al., ibid.* 4875.

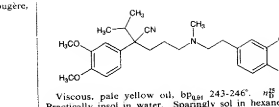


Crystals from ethanol, mp 119-123° and 165-169°; $[\alpha]_D^{28}$ −84.1° ±3 (*c* = 0.533 in $CHCl_3$).

*N,O,O*-Triacetate, mp 152-154°. $[\alpha]_D^{26}$ −8.0° ($CHCl_3$)

*N*-Monoacetate, mp 191-193°. $[\alpha]_D^{26}$ −79.1° ($CHCl_3$).

**10083. Verapamil.** *α-[3-[[2-(3,4-Dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy-α-(1-methylethyl)-benzeneacetonitrile; 5-[(3,4-dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile;* α-isopropyl-α-[(*N*-methyl-*N*-homoveratryl)-γ-aminopropyl]-3,4-dimethoxyphenylacetonitrile; iproveratril; D-365. $C_{27}H_{38}N_2O_4$: mol wt 454.61. C 71.34%, H 8.43%, N 6.16%, O 14.08%. Coronary vasodilator with calcium blocking activity. Prep: **Belg.** pat. **615,861;** Dengel, U.S. pat. **3,261,859** (1962, 1966 both to Knoll). Physical and chemical data: Appel, *Arzneimittel-Forsch.* **12,** 562 (1962). Synthesis and absolute configuration of enantiomers: Ramuz, *Helv. Chim. Acta* **58,** 2050 (1975). Stereospecific synthesis of enantiomers: L. J. Theodore, W. L. Nelson, *J. Org. Chem.* **52,** 1309 (1987). Pharmacology: Haas, Hartfelder, *ibid.* 549; Schleyer, Witzleb, *ibid.* 559. Metabolism: Mellhenny, *J. Med. Chem.* **14,** 1178 (1971). HPLC determin in plasma: C. Horne *et al., Arzneimittel-Forsch.* **37,** 956 (1987). Series of articles on clinical studies: *ibid.* **20,** 1277-1336 (1970). Comparative study in variant angina: D. D. Waters *et al., Am. J. Cardiol.* **47,** 179 (1981); in arrhythmias: B. N. Singh *et al., Drugs* **25,** 125 (1983). Symposium on pharmacology and clinical efficacy in hypertension: *Am. J. Cardiol.* **57,** 1D-107D (1986). Comprehensive description: Z. L. Chang, *Anal. Profiles Drug Subs.* **17,** 643-674 (1988). *Reviews:* S. H. Baky, E. B. Kirsten, in *Pharmacological and Biochemical Properties of Drug Substances* **vol. 3,** M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1981) pp 226-261; D. J. Triggle, V. C. Swamy, *Circ. Res.* **52**(2), Pt. 2, 117-128 (1983).

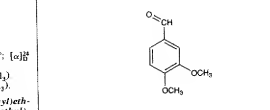


Viscous, pale yellow oil, $bp_{0.01}$ 243-246°. $n_D^{25}$ 1.5448. Practically insol in water. Sparingly sol in hexane; sol in benzene, ether. Freely sol in the lower alcohols, acetone, ethyl acetate, chloroform.

Hydrochloride, $C_{18}H_{29}NO_4$.HCl. *Arpamyl, Berkatens, Calan, Cardiagut, Cardibeltin, Cordilox, Dignover, Droxteakard, Geangin, Isoptin, Quasar, Securon, Univer, Vasolan, Veracim, Veramex, Verapin, Verelan, Verocamil.* Crystals: dec 138.5-140.5° (corr). Sol (21°): 7 g/100 g water (pH 4.24). pH of 0.1% aq soln: 5.25. uv max: 232, 278 nm. Sparingly sol in chloroform. Sol in ethanol, isopropanol, acetone, ethyl acetate; freely sol in methanol, DMF. Soly (mg/ml): water 83, ethanol (200 proof) 26, propylene glycol 93, ethanol (190 proof) > 100, methanol > 100, 2-propanol 4.6, ethyl acetate 1.0, DMF > 100, methylene chloride > 100, hexane 0.001. pKa 8.6. $LD_{50}$ in rats, mice (mg/kg): 16, 8 i.v. (Baky, Kirsten).

THERAP CAT: Antianginal; antiarrhythmic (class IV).

**10084. Veratraldehyde.** *3,4-Dimethoxybenzaldehyde;* 3,-4-dimethoxybenzenecarbonal; veratric aldehyde; protocatechualdehyde dimethyl ether. $C_9H_{10}O_3$: mol wt 166.18. C 65.05%, H 6.07%, O 28.88%. Prepd by methylation of vanillin: Kostanecki, Tambor, *Ber.* **39,** 4022 (1906); Buck, *Org. Syn.* **13,** 102 (1933); Alt, U.S. pat. **3,007,968** (1957 to Monsanto); by oxidation of veratryl alcohol with chromium(VI) oxide-pyridine complex: Holum, *J. Org. Chem.* **26,** 4814 (1961).



Needles from ether, petr ether, toluene, or carbon tetrachloride. Odor of vanilla beans; mp 42-43°; $bp_{766}$ 281°; $bp_{53}$ 201°; $bp_{18}$ 155°. Slightly sol in hot water; freely sol in alcohol and ether. Solns are oxidized to veratric acid under the influence of light.

**10085. Veratramine.** *(3ß,23ß)-14,15,16,17-Tetradehydroveratraman-3,23-diol.* $C_{27}H_{39}NO_2$: mol wt 409.61. C 79.17%, H 9.60%, N 3.42%, O 7.81%. Secondary base from *Veratrum grandiflorum* (Maxim.) Loes. f., and from *V. viride* Ait., *Liliaceae.* Isoln and structure: Saito, *Bull. Chem. Soc. Japan* **15,** 22 (1940); Jacobs, Craig, *J. Biol. Chem.* **160,** 555 (1945); Jacobs, Sato, *ibid.* **181,** 55 (1949); **191,** 71 (1951); Tamm, Wintersteiner, *J. Am. Chem. Soc.* **74,** 3842 (1952); Wintersteiner, *Festschrift Arthur Stoll* (Birkhäuser-Verlag, Basel) pp 166-176. Total synthesis: Masamune *et al., J. Am. Chem. Soc.* **89,** 4521 (1967); Johnson *et al., ibid.* 4523; Masamune *et al., Tetrahedron* **27,** 3369 (1971); Kutney *et al., Can. J. Chem.* **53,** 1796 (1975). Stereochemistry Sicher, Tichy, *Tetrahedron Letters* **1959**(12), 6 (1959); Kataoka, *Chem. & Ind. (London)* **1961,** 512; Bailey *et al., Tetrahedron Letters* **1963,** 555. Revised stereochemistry: Scott *et al., ibid.* **1967,** 2381; Kupchan, Suffness, *J. Am. Chem. Soc.* **90,** 2730 (1968); Sprague *et al., Tetrahedron* **27,** 4857 (1971). *See also:* Veratrum Viride.